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# (54) Diagnostic aid

(57) A pen-shaped holder 1 is used to mount detachable strip, or needle, electrode carriers, its shape and nature permitting delicate manipulation to attach and detach the small carriers from an electrical socket 3 at one end. On these strips or needles are small electrodes sensitive, e.g. to blood glucose by containing a glucose-catalytic enzyme (oxidase, dehydrogenase) and a mediator compound such as ferrocene to give an electrical signal corresponding to the catalytic reaction e.g. with blood glucose as a diagnosis or control tool for diabetes. The pen-shaped holder has a digital readout 6 corresponding to the measurement, located towards its other end, and contains a battery 8 and operating circuitry 9.

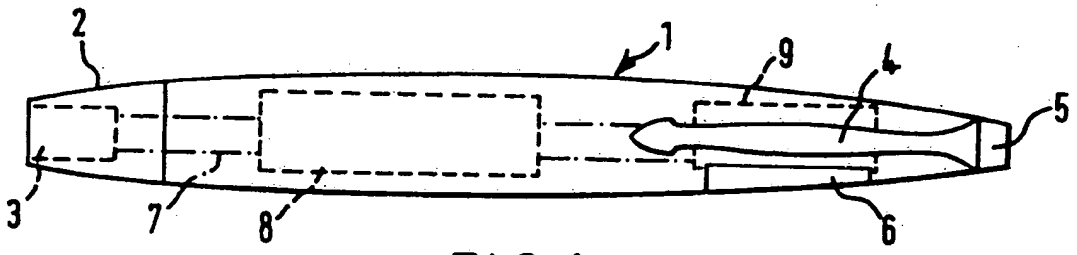


FIG.1a.

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The drawings originally filed were informal and the print here reproduced is taken from a later filed formal copy.

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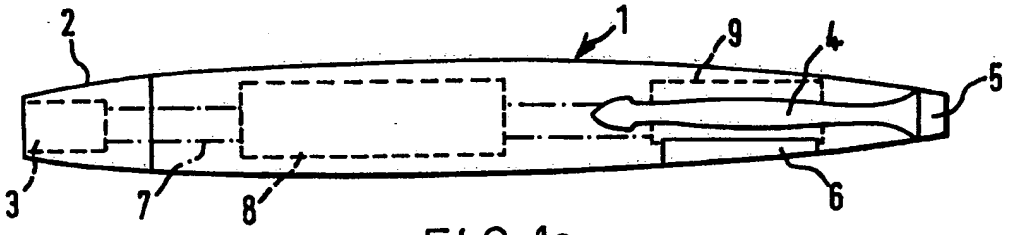


FIG. 1a.

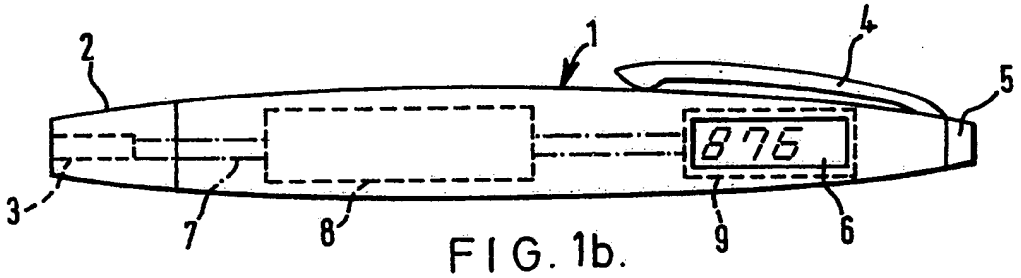


FIG. 1b.

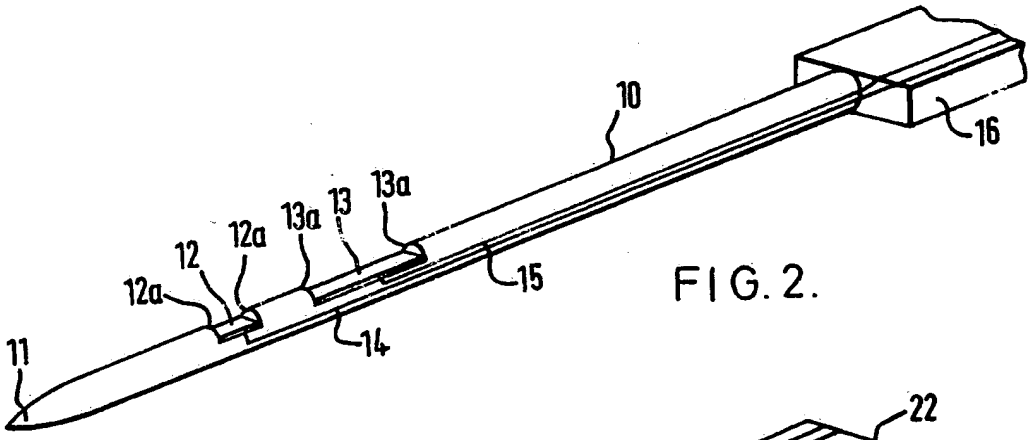


FIG. 2.

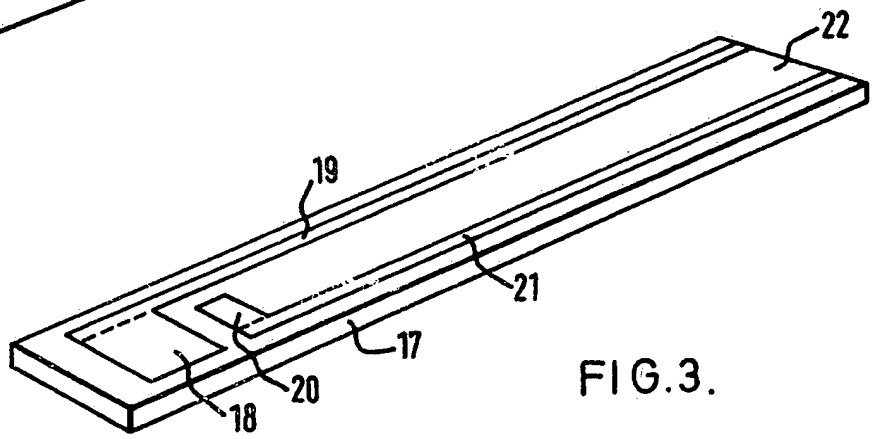


FIG. 3.

SPECIFICATION

**Diagnostic aid**

This invention relates to equipment giving a visible readout correlated with a selected physiological parameter thus being capable of use in human or veterinary medicine by medical or nursing personnel, or by experienced lay subjects on a self-measurement basis.

One type of such equipment (to which the present invention is not generally limited) is based on the inventions described in copending patent Applications assigned to the same assignee as the present application. These applications describe inter alia numerous types of enzyme-coated electrodes each specific to the presence of a physiological or other substrate for which the particular enzyme acts as a catalyst and each therefore potentially capable of acting to detect, measure or monitor the level of the substrate *in vivo* or *in vitro* and give a readout correlated with an underlying physiological condition controlling or affecting the substrate level. By way of example, use of glucose oxidase or bacterial glucose dehydrogenase as the enzyme, associated with suitable electron-transferring mediator compounds, has been shown to give readout signals correlating linearly with *in vitro* blood glucose levels over a wide range thus giving a diagnostic or measuring tool for diabetic conditions. For convenience, this document will refer hereinafter to such blood-glucose-measuring equipment as being typical but not limitative of equipment with which the present invention is concerned.

Diabetic subjects need to measure their glucose levels frequently. Hitherto, a common method carried out by the subject personally is a colourimetric test using a blood or urine sample which is applied over a surface area containing a colour-reactive detector chemical, adjacent to a comparison area ,to give a colour change which is compared with a chart of colour values as an approximate measure of glucose level.

There are however defects in this method. Firstly, colourimetric changes are notoriously difficult to assess, especially if the patient has impaired vision as a result of the diabetic condition. Indeed, because of this problem expensive automatic colour comparison equipment may need to be purchased by some subjects for interpreting the test results. Secondly, the blood test, while inherently more accurate than a urine test, needs a large enough sample to cover both the test surface and the comparison surface. Since blood samples, on a self-treatment basis are taken from body extremities (fingers, toes, earlobes) they are normally not inherently large enough when obtained by a simple needle-prick, and must in fact be expressed i.e. squeezed or massaged out to form a larger drop. progressively, the tissue of the extremities becomes scarred and coarsened by such treatment to an extent whereby finding fresh testing sites presents a problem.

In order to embody, on a home-diagnostic basis the invention described in our earlier patents, this invention in one aspect is directed to provision of small scale non-traumatic test pieces, either as a small-diamete invasive probe electrode or as an external test electrode strip capable of using the naturally-arising small blood droplet from a needle-prick tester, without tissue massage. Examples are described in more detail below.

These small-scale electrodes are intended as single-use throwaway articles and are utilized in conjunction with electrical circuitry and a readout means, to which they must be easily attachable and detachable. Such circuitry and readout means is itself preferably embodied on a very small scale.

We have accordingly found that the totality of the equipment is subject to certain design constraints, e.g.:

(i) it should be nontraumatic to the user either physically e.g. if used with its own invasive probe or psychologically by virtue of its appearance,

(ii) it should be capable, despite the small size of the throwaway electrode and of the permanent circuitry/readout components, of easy assembly and disassembly even by juvenile or elderly lay users,

(iii) the relatively expensive permanent circuitry/readout components should, despite their small size, be of a form which minimizes loss or damage and,

(iv) the display readings should be visible and understandable to a lay user.

We have now found that these criteria can be fulfilled by assembling the circuitry/readout components into a housing resembling a pen/digital-watch.

According to one aspect of the present invention there is provided an assembly of circuitry and display means for use in producing a readout value as a diagnostic aid in human or veterinary medicine, housed in a pen-like, hollow elongate housing having (a) at one end an electrically conductive socket suitable to receive the outer end of at least one detachable test member capable of producing an electrical signal correlating with a physiological parameter to which the test member is selectively sensitive and (b) towards the other end a digital read-out window for exhibiting a numerical value corresponding to the parameter.

The man skilled in the art of designing medical equipment will appreciate that the invention extends not only to the pen-like assembly as defined above but also to the combination of such an assembly with an attached test member, and to the combination as a kit of interrelated parts of such an

assembly with a plurality of test members suitable for one-off use.

The term "pen-like" is a general limitation on size and shape. In functional terms, its characteristics are such that it can be held near the socket between the thumb and the nearer one or two opposed fingers, with the elongate body resting on and extending beyond the forefinger, but not to an extent that prejudices fine control of the socket end by the thumb and fingers. In numerical terms it can be from 10 to 30 cms. long and from 0.5 to 3 cms. across its maximum transverse dimension; more usually it will be from 12 to 20 cms. long and from 0.8 to 1.5 cms. across. It can be generally circular, or polygonal, in cross-section. Each detachable test member is usually a small-scale enzyme-coated sensor electrode, of the type discussed in the earlier Patent Applications listed above, and especially such an electrode where the enzyme is specifically glucose-catalyzing whereby diabetic conditions can be measured. It may be a small-calibre invasive probe e.g. based on a 27-gauge needle familiar to diabetics. It may alternatively be a flat external strip electrode dimensioned to operate on a small, non-expressed, blood droplet. The socket arrangement will vary accordingly.

In one embodiment of the present invention, two or more sensor electrodes may be incorporated into a single test member, again ,the socket arrangement will vary accordingly.

The readout means will typically be a conventional seven-segment display window towards the rearward end of the 'pen' as in conventional pen/watches. In the case of the multiple sensor embodiment described in the preceeding paragraph the display may be switchable between each sensor's discrete monitoring circuit, both the display and a single monitoring circuit may be switchable between sensors, or, a specific display may be provided for each of the sensors present.

In another aspect the invention provides a needle probe member for placement through tissue into a measurement location such as a blood vessel, in the form of a generally cylindrical pointed needle (preferably of a standard size e.g. 27-gauge) having formed therein near the pointed end two flat depressions spaced apart longitudinally, each depression with a floor at right angles to the needle radius and each with a protective shoulder at each end of that floor: wherein the floor of one such depression is coated with an adherent electrode layer capable of producing an electrical signal correlating with a physiological parameter to which the electrode layer is selectively sensitive; the floor of the other such depression is coated with an adherent reference electrode layer; and separate conductive elements are provided along the surface of the needle, communicating one with each electrode layer, for connection to signal readout means attachable at the outer end of the needle. As will be apparent from the general disclosure herein, it is envisaged that in one form sensitive and selective electrode may comprise a glucose hydrogenase (or oxidase) enzyme associated with ferrocene or a like compound as a mediator compound. The reference electrode can be silver/silver chloride. The shoulders (one to each end of the depression), because of the small overall probe size, protect the electrode coatings as the needle passes through tissue e.g. into a vein.

In yet another aspect the present invention provides a strip test electrode comprising (a) a flat electrode area of known area small enough to be completely coverable by the smear of blood produced from a non-expressed drop of blood generated from a needle-prick at a bodily extremity, the electrode being of a composition capable of producing an electrical signal correlating with a phsiological parameter to which the electrode layer is selectively sensitive (b) a reference electrode area separate from but sufficiently close to the sensitive electrode area that the said blood smear also reaches the reference electrode to establish electrical communication and (c) separate conductive elements extending along the surface of the strip, communicating one with each electrodes for connection to signal read-out means-attachable to one end of the strips.

The "sensitive" electrode may again comprise a glucose dehydrogenase (or oxidase) enzyme associated with ferrocene or a like compound as a mediator, and the reference electrode may be a silver/silver chloride reference electrode. The area of the sensitive electrode is generally substantially square; it may be rectangular or otherwise shaped, but in any case usually will correspond in area to a square of 5 mm edge length, or below, e.g. from 2 to 4 mm.

The invention will be further described with reference to the accompanying drawings, in which:

Figures 1*a* and 1*b* are general diagrammatic side views of a pen-like holder housing an assembly of circuitry and having a readout-window.

Figure 2 shows a probe electrode capable of use with the holder of Fig. 1, and

Figure 3 is a strip electrode capable of use with the holder of Fig. 1.

From above the holder 1 intentionally resembles a conventional pen/watch as much as possible. It has a forward end 2, possibly rotary to tighten the walls of a flattened socket cavity 3 formed within it. A central join, a clip 4 and a press-button 5 all resemble those of a conventional pen, and digital readout-window is also of a type known in pen/watches.

Inside the holder as shown by dotted lines

is connection circuitry 7, possibly printed in situ, battery 8 and operating circuitry 9 behind and manufactured as a unit with the display window 6. The display can be capable of operation only when button 5 is pressed so that extra illumination can be provided if necessary.

Fig. 2 shows a 27-gauge (0.3 mm) needle 10 pointed out at 11 and having a smaller area 12 and a larger area 13 cut from its curved surface as shown. Area 12 is coated with silver to provide a reference silber-silver chloride potential. Area 13 is coated first with carbon and thereafter with a mediator compound such as ferrocene and with a glucose-sensitive enzyme e.g. bacterial glucose dehydrogenase. A protective membrane can if desired also be located over this deposit. It is to be observed that the recess area 13 is a well-defined area of accurate size; also that the shoulders 12a and 13a protect the respective deposits located between them as the needle is passed through tissue.

Deposited conductive lines 14 and 15 pass separately along needle 10 and over its shaped end 16, the exact path of the these lines not being of major significance except that they should not touch and that they should only connect one way round if head 16 lies in socket cavity 3 (Fig. 1).

Fig. 3 shows a strip electrode 17 made of, for example, a ceramic material or printed-circuit-board laminate. It includes a square area 18 with connector lead 19, the square area being covered with the enzyme-containing layers as described above. It further includes a small reference electrode area 20 and separate connector lead 21. The rearward end 22 of the electrode 17 fits into a socket as at 3. It is to be noted that, as with the needle 10, the electrode strip 17 is a small-scale device. Thus square area 18 is of a side length only about half that of each of two square colourimetric test areas of conventional diagnostic tests and can be used with the original non-expressed bead of blood from a needle-prick device,which is adequate to cover the whole of the square area and communicates electrically with reference electrode area 20.

The embodiments shown fulfill the design criteria listed above.

The delicate manipulation facilitated by the pen grip (e.g. by thumb and finger) means that the small electrodes can be easily assembled into, or detached from, the socket. A user will always orient the holder with the window visible thus always giving a uniform relative orientation to the socket whereby the rearward ends of the fragile electrodes can be fitted without experiment and damage.

The "pen" format is instinctively picked up after use and safely carried in a pocket, more so than for any other small device. Thus the expensive part of the equipment is safeguarded. Furthermore, it is possible to incorporate a conventional timer circuit into the device thereby fulfilling the actual function of a pen-type watch and providing an audible or visible signal which marks the point in time at which a reading should be taken

Finally, the display is numerical, clearly visible and if necessary can be supplemented by an illuminating light source.

## CLAIMS

1. An assembly of circuitry and display means for use in producing a readout value as a diagnostic aid in human or veterinary medicine, housed in a pen-like hollow elongate housing having;

(a) at one end an electrically conductive socket suitable to receive the outer end of at least one detachable test member capable of producing an electrical signal correlating with a physiological parameter to which the test member is selectively sensitive and,

(b) towards the other end a digital read-out window for exhibiting a numerical value corresponding to the parameter.

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